Written statement to the

U.S. Congressional Committee on Energy and Commerce

Subcommittee on Health

Hearing on "21st Century Cures: The President's Council of Advisors on Science and Technology (PCAST) Report on Drug Innovation"

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Members of the Committee:

I am Dr. Raymond Woosley, President of AZCERT, a non-profit organization created to foster the safe use of medicines. I have over 35 years of experience in academia, the pharmaceutical industry and in the non-profit sector. The greater part of my career in clinical pharmacology and cardiology has been spent creating inter-professional and inter-disciplinary programs to improve medical outcomes with medications. I have led federally funded programs in clinical research such as the General Clinical Research Center at Georgetown (now termed CTSA's) and an AHRQ funded Center for Education and Research on Therapeutics (CERTs) in Arizona. I was formerly Vice-President and Dean of the College of Medicine at the University of Arizona and in 2005 I left to found the Critical Path Institute (C-Path), a partnership between the FDA, the biopharmaceutical industry and academic scientists dedicated to developing consensus on best practice methods in drug development. These experiences have convinced me that partnerships and inter-disciplinary approaches are not only effective, they must be at the core of our national plan for biomedical innovation.

Like many previous reports, the 2012 PCAST report summarizes the serious problem that was first recognized almost a decade ago when FDA Commissioner Dr. Mark McClellan called attention to the declining number of innovative new medical products being submitted to the FDA, in spite of a 250% increase in the nation's research and development (R&D) investment. Today, the United States invests over $30 billion each year in NIH-funded research, more than the rest of the world combined, yet, only 30-40 innovative new medications reach the market each year. In fact, the number is essentially unchanged since 1975. Doubling of the NIH budget and increasing investments in pharmaceutical R&D have not changed the number of truly innovative new drugs that reach patients each year.

The PCAST report set as a national goal the doubling of the number of innovative new biomedical products that reach the market over the next 10-15 years. Considering the combined $100 Billion spent annually for biomedical R&D by industry and the federal government, this seems to be a terribly modest target, one that is not substantially different from the status quo. However, we cannot even assume that the status quo will not become worse. Figure one in the PCAST report shows that since 2008, pharmaceutical investments in R&D are in decline. The status quo, however unpleasant, may not continue if biopharmaceutical investment continues to decline and other changes are not made.

The first recommendation in the report calls for continued support of basic biomedical research, NCATs and the Reagan-Udall Foundation (RUF). In addition to NCATS and RUF, there are many other important federal programs that now have minimal funding and are just as important for completing the innovation "supply chain" as discussed below. The PCAST report calls for creating yet another under-funded super-committee, a broad based Partnership to Accelerate Therapeutics (PAT). The report likens the PAT to the Institute of Medicine's Drug Forum but anticipates that it will be more

successful. Experience with this, and previous under-funded, broadly represented discussion forums, would argue that the PAT will not have substantive impact.

The PCAST report failed to propose any bold initiatives that could have meaningful impact on the mammoth problem at hand or that could even reach the report's modest target of doubling the current low level of productivity of the biomedical research enterprise. It discusses, but discounts, the only bold alternative that was raised by the PCAST consultants, i.e. a SEMATECH for biopharmaceutical development. Perhaps it could be named "BIOTECH". Bold initiatives are often suppressed because funding is unlikely or they threaten powerful stakeholders who are inextricably wed to the current paradigm. The question is not whether a SEMATECH-like organization is needed but… What would it do? SEMATECH was not a convener nor was it simply a forum for discussion of the problem. It brought scientists from government, industry and academia together to identify the reasons why US-made computer chips were failing and it employed applied science solutions such as establishing manufacturing standards and defining best practices. It did not compete with the established organizations working in the field. It brought them into the improvement process and utilized their unique skills and expertise.

An empowered and inclusive BIOTECH could restructure the nation's current investment which is grossly imbalanced toward discovery science ($30 billion) on one end and market approval (over $46 billion) on the other. As shown below, nine other essential links in the supply chain share less than $600 million in support. The following are my rough estimates of current funding across the innovation supply chain (Color added for emphasis of funding gap):

- Discovery: $30 billion (NIH)

- Replication/Validation of discovery: $ 40 million by the Accelerated Medical Partnership (AMP)
- Translational research on mechanism of disease: $ 485 million at NCATS & Cures Action Network
- Biomarker discovery: $ 30 million by TransCelerate Biopharma and FNIH's biomarker consortium
- Biomarker qualification & best practices in R&D: $ 5 million for Critical Path Public Private Partnerships by FDA
- Regulatory Science: < $ 5 million by FDA, NIH and RUF
- Data Standards for clinical research: < $5 million by CDISC
- Biological Standards for biomarker assays: < $5 million by NIST
- Training of Clinical Investigators: < $20 million by NIH
- Methods for post-market surveillance: < $10 million by AHRQ and FDA (mini-Sentinel)

- Development: $45 Billion by biopharma industry
- Review and approve new products: $1.2 billion for FDA review(includes user fees)

Each of these roles is an essential element in an efficient and productive supply chain for discovery, development and marketing of innovative new products. Any under-resourced element in the chain is its weakest link, and there are several.

I believe that the funding gap between discovery and development shown above is a major contributor to the "valley of death" for new products.

What could a balanced, inter-linked ecosystem do to support development of scientific discoveries and enable new product development?

1. Create confidence in the discovery – make validation of biomarkers and drug targets as the first critical step in the discovery process (a discovery that cannot be replicated is not a discovery but an expensive distraction)
2. Understand diseases at the molecular level – research networks that study and understand the mechanism of disease
3. Know exactly who has the disease of interest - Registries that define and identify the sub-populations appropriate for testing with new candidate therapies.
4. Identify biomarkers of drug action that are founded on solid, cutting edge science and measured using reproducible, standardized methods.
5. Identify methods of drug testing and development that are "best of breed" and accepted by a consensus that includes multiple developers and regulatory agencies.
6. Establish common data elements for clinical research that bring greater efficiency to analysis of data from multiple sources and enable modeling and simulation of development strategies.
7. Create tools and infrastructure in medical practice that enable rapid learning in order to determine whether innovations are safe, have efficacy and are cost effective.

What can BIOTECH deliver: A balanced, synchronous approach to development

Bringing balance and synchrony to the supply chain continuum will require either new or redirected federal funding. Synchrony will require a forum for open dialog, scientific interchange and the authority to set priorities, to define technical standards and to identify best practices in development. SEMATECH provided the semiconductor industry with that forum and the required synchrony. For SEMATECH, Congress and the semiconductor industry shared the burden of funding. Congress and the biopharmaceutical industry should unite to bring all stakeholders working in the supply chain under the umbrella of BIOTECH.

If given the authority and the resources, BIOTECH could play an essential role by assuring that each element in the chain is seamlessly connected and has the necessary funding to produce the applied science and the development tools that are needed by developers.

Candidate organizations and their potential roles within BIOTECH could include:

- FNIH – raise funds to perform specific projects of interest to BIOTECH and the NIH, especially NCATS
- Reagan-Udall Foundation – raise funds to perform specific projects of interest to BIOTECH and FDA
- CDISC – Establish data standards for clinical research and disease data elements
- NIST – Establish performance standards for laboratory methods to assay biomarkers
- C-Path – Establish consensus between regulators and developers for best practices in testing and evaluation of new drugs
- NCATS (CTSAs) – Establish clinical research networks and registries for specific illnesses
- CDC drug surveillance program – Establish post-market drug/biologic/device surveillance (Sentinel system)

A balanced supply chain approach will require a focus on better funding for applied science, modernization of the research infrastructure, technology standards and verification of scientific validity at all stages of the innovation supply chain. It will require investment in healthcare practice environments in order to make it a truly learning healthcare environment for rapid testing and development of new medical products. The use of clinical trial networks and patient registries, already of proven value, should be made integral components of medical practice. Innovative approaches to rapid and efficient learning from research such as Vanderbilt Medical Center's clinical research program should be the norm for the nation. Such changes require a bold vision such as a SEMATECH for biopharmaceuticals. i.e. BIOTECH.

Thank you for the opportunity to present this recommendation to the Committee.

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